

modifications L351Y, F405A, and Y407V, and said second CH3 domain polypeptide comprising amino acid modifications T366L, K392L, and T394W. In a further embodiment is the isolated heteromultimer Fc construct described herein, said first CH3 domain polypeptide comprising amino acid modifications L351Y, F405A, and Y407V, and said second CH3 domain polypeptide comprising amino acid modifications T366L, K392M, and T394W. In some embodiments is the isolated heteromultimer Fc construct described herein, said first CH3 domain polypeptide comprising amino acid modifications L351Y, F405A, and Y407V, and said second CH3 domain polypeptide comprising amino acid modifications T366L, K392L, and T394W. In certain embodiments is the isolated heteromultimer Fc construct described herein, wherein at least one of said first and second CH3 domain polypeptides is a modified CH3 domain polypeptide comprising an amino acid modification at position S400. In a further embodiment is the isolated heteromultimer Fc construct described herein, comprising the modification S400Z, wherein Z is selected from a positively charged amino acid and a negatively charged amino acid. In some embodiments, the positively charged amino acid is lysine or arginine and the negatively charged amino acid is aspartic acid or glutamic acid. In certain embodiments is the isolated heteromultimer Fc construct described herein, said first CH3 domain polypeptide comprising an amino acid modification selected from S400E and S400R. In some embodiments is provided the isolated heteromultimer Fc construct described herein, wherein at least one of said first and second CH3 domain polypeptides is a modified CH3 domain polypeptide comprising an amino acid modification at position N390. In some embodiments, the modification of N 390 is N390Z, wherein Z is selected from a positively charged amino acid and a negatively charged amino acid. In an embodiment, N390Z is N390R. In certain embodiments of the isolated heteromultimer Fc construct described herein, said first CH3 domain polypeptide is a modified CH3 domain polypeptide comprising the amino acid modification S400E and said second CH3 domain polypeptide is a modified CH3 domain polypeptide comprising the amino acid modification N390R. In some embodiments of the isolated heteromultimer Fc construct described herein, each of the first and second CH3 domain polypeptide is a modified CH3 domain polypeptide, one said modified CH3 domain polypeptide comprising the amino acid modification Q347R and the other modified CH3 domain polypeptide comprising the amino acid modification K360E.

[0006] Provided in one aspect is an isolated heteromultimer Fc construct comprising a modified heterodimeric CH3 domain, said modified CH3 domain comprising: a first modified CH3 domain polypeptide comprising at least three amino acid modifications as compared to a wild-type CH3 domain polypeptide, and a second modified CH3 domain polypeptide comprising at least three amino acid modifications as compared to a wild-type CH3 domain polypeptide; wherein at least one of said first and second CH3 domain polypeptides comprises an amino acid modification of K392J wherein J is selected from L, I or an amino acid with a side chain volume not substantially larger than the side chain volume of K; wherein said first and second modified CH3 domain polypeptides preferentially form a heterodimeric CH3 domain with a melting temperature (T_m) of at least about 74° C. and a purity of at least 95%; and wherein at least one amino acid modification is not of an amino acid

which is at the interface between said first and said second CH3 domain polypeptides. In certain embodiments is a heteromultimer Fc construct described herein, comprising at least one T350X modification, wherein X is a natural or non-natural amino acid selected from valine, isoleucine, leucine, methionine, and derivatives or variants thereof. In some embodiments is an isolated heteromultimer Fc construct described herein, comprising at least one T350V modification. In an embodiment is an isolated heteromultimer Fc construct described herein, wherein the modified CH3 domain has a melting temperature (T_m) of at least about 75° C. or greater. In an embodiment is the isolated heteromultimer Fc construct described herein, wherein the modified CH3 domain has a T_m of about 77° C. or greater. In certain embodiments, the modified CH3 domain has a T_m of about 80° C. or greater. In an embodiment is the isolated heteromultimer Fc construct described herein, wherein at least one CH3 domain polypeptide is a modified CH3 domain polypeptide comprising an amino acid modification of at least one of K409 and T411. In certain embodiments is the isolated heteromultimer Fc construct described herein, comprising at least one of K409F, T411E and T411D. In some embodiments is the isolated heteromultimer Fc construct described herein wherein at least one CH3 domain polypeptide is a modified CH3 domain polypeptide comprising an amino acid modification of D399. In some embodiments, the amino acid modification of D399 is at least one of D399R and D399K.

[0007] Provided in one aspect is an isolated heteromultimer Fc construct comprising a modified heterodimeric CH3 domain, said modified CH3 domain comprising: a first modified CH3 domain polypeptide comprising at least three amino acid modifications as compared to a wild-type CH3 domain polypeptide, and a second modified CH3 domain polypeptide comprising at least three amino acid modifications as compared to a wild-type CH3 domain polypeptide; wherein at least one of said first and second CH3 domain polypeptides comprises an amino acid modification of K392J wherein J is selected from L, I or an amino acid with a side chain volume not substantially larger than the side chain volume of K; wherein said first and second modified CH3 domain polypeptides preferentially form a heterodimeric CH3 domain with a melting temperature (T_m) of at least about 74° C. and a purity of at least 95%; and wherein at least one amino acid modification is not of an amino acid which is at the interface between said first and said second CH3 domain polypeptides. In certain embodiments is a heteromultimer Fc construct described herein, comprising at least one T350X modification, wherein X is a natural or non-natural amino acid selected from valine, isoleucine, leucine, methionine, and derivatives or variants thereof. In some embodiments is an isolated heteromultimer Fc construct described herein, comprising at least one T350V modification. In an embodiment is an isolated heteromultimer Fc construct described herein, wherein the modified CH3 domain has a melting temperature (T_m) of at least about 75° C. or greater. In an embodiment is the isolated heteromultimer Fc construct described herein, wherein the modified CH3 domain has a T_m of about 77° C. or greater. In certain embodiments, the modified CH3 domain has a T_m of about 80° C. or greater. In certain embodiments of the isolated heteromultimer Fc construct described herein, wherein the first CH3 domain polypeptide is a modified CH3 domain polypeptide comprising at least one amino acid